Update on Major IPV Initiatives

Polio Immunization: Moving Forward,
Bethesda, 19-20 September 2007

Overview

- Convene Polio Research Subcommmittee
- Major initiatives:
  - Assessment of emerging polio risks
  - Research to accelerate eradication
  - Long-term containment of polioviruses
  - Long-term surveillance and response
  - Research on safer and more affordable IPV
    - S-IPV development
    - IPV demonstration project
    - Schedule- and dose reduction studies
  - Options for OPV cessation
- Program of work for Inactivated Poliovirus Vaccine (IPV)
- Summary/conclusions

IPV Program of Work

- **Better define epidemiology**
  - Policy changes: New Zealand, Australia
  - Borders between OPV and IPV: US-Mexican border study
  - Demonstration projects: Switch from OPV to IPV (Argentina, Mexico, Indonesia)
- **Develop IPV policy** (April 2006: IPV following OPV cessation)
  - IPV requirements for countries electing to retain poliovirus after OPV cessation
  - Concept of secondary safe guards (incl. vaccination requirements introduced into GAP-III)
  - Immunogenicity of IPV (especially contribution of 4th dose)
- **New vaccine/seed strain development**
  - Sabin-IPV
- **Schedule- and dose reduction studies**
  - Fractional IPV dose studies under way in Cuba and Oman

Sabin-IPV Development

Sabin-IPV Rationale

- Facilitate containment
- Serve as "warm-base" for restart OPV production
- Minimize the proliferation of wild poliovirus amplification sites
- Facilitate the replacement of wild poliovirus in vaccine production (longterm objective)
- Roadmap for development of new seed strains for IPV production

IPV Demonstration Project

Project Outline

- 5-year demonstration project of IPV introduction into a tropical area
- Collaboration between MOH, Provincial Health, vaccine manufacturer & WHO
- Yogjakarta province (population ~5 million; birth cohort ~55,000)

Objectives

- **GENERAL OBJECTIVES**
  - to assess the operational feasibility of using an IPV-only schedule for the prevention of poliomyelitis; and
  - to evaluate the scientific and programmatic issues affecting the use of an IPV-only schedule in a tropical developing setting.
- **SPECIFIC OBJECTIVES**
  - will IPV-induced immunity prevent OPV-derived virus from establishing circulation; and
  - how many doses of IPV provided at which age (and interval) will be necessary to induce immunity to polioviruses in a high proportion (>90%) of vaccinees.

Feasibility Completed

- Vaccination coverage (**done**):
- Environmental surveillance (**established 1 July 04**):
- Ethical review (**done**):
- Majelis Ulama Indonesia (MUI) (**decision made with Sharia Division, MOH**):

Environmental Surveillance

- Weekly sample collection began in early July 2004 in Yogyakarta
- Samples processed yielded pos
(Sabin polioviruses)
- Sample 7 results (part) below

Project started & Proceeding well!

Collection site	Sample code	Date of collected sample	Date of sample send to lab.	Date of sample received at lab.	S condition	no					Non Polio EnteroVirus	Date of send the result
Inlet sewage	IPV 007/08/04	23/8/2004	23/8/2004	24/8/2004	Good	007	L	1				16/9/2004
IPAL Sewon Bantul								2				
								3				
								4	n			
								5	pos.	Polio 2		
							RI	1	pos.		Not done	

- First shipment of concentrates and tissue cultures to GSL/Finland (done, end of September)
- Protocol for NPEV (drafted already)

Immunization Strengthening

- Immunity assessment (**done**)
- Serological survey (before (**done**) / and year after IPV introduction; contribution of 4th dose)
- Cold chain capacity assessment (**done**):
  - Cold chain expert to review & prepare report
- Communication plan (**done**):
  - Including advocacy, social mobilization, sensitization, and training (incl. medical associations, universities, NGOs, ..)

Vaccination Policy

- Vaccines:
  - Vaccine (IPV)
  - Note: DTP-HB introduced early 2005

Age	Now	Future
0-1 m	BCG, OPV, HB	BCG, HB
2 m	OPV, DTP, HB	IPV, DTP-HB
3 m	OPV, DTP, HB	IPV, DTP-HB
4 m	OPV, DTP, HB	IPV, DTP-HB
9 m	measles	IPV, measles

Status & Next Steps

- **A two-year delay (calamities: tsunami, earth quake; and polio outbreak following importation)**
- **IPV introduction phase completed**
  - Vaccine procurement (donation)
- **Plans of action finalized (including communication & training)**
- **Memorandum of Understanding (MOU) signed**
  - Government, Province & WHO
- **Switch from OPV to IPV has occurred, 3 September 2007**

Schedule- and Dose Reduction Studies for IPV

Objective and Rationale for Schedule- and Dose Reduction

- **Objective of Program-of-Work**:
  - Provide the option for IPV use to decision-makers in lower-middle and low-income countries
- **Rationale:**
  - Routine Use:
    - Make IPV potentially affordable to lower-middle and low-income countries (combination IPV vaccines expensive)
  - Campaign Use:
    - Stretch limited supplies of IPV
    - Limit expenses
    - Facilitate administration of IPV by volunteers in large-scale campaigns

Lines of Interest/Investigation

- Reduced schedule:
  - 2-dose schedule with IPV in Senegal administered 6 months apart provided a efficacy of 90% → literature review
- Fractional doses:
  - 1/5 dose of IPV (0.1 ml) administered intradermally provides similar seroconversion than full doses → clinical trials

Robertson S, et al. Clinical efficacy of a new enhanced-potency inactivated poliovirus Vaccine. Lancet 1988;i:897-899.

Samuel BU,et al. Immune response to intradermally injected inactivated poliovirus vaccine. Lancet 1991;338:343-4. Nirmal S et al. Immune response of infants to fractional doses of intradermally administered inactivated poliovirus vaccine. Vaccine 1998;16:928-31.

Table 2. Immunogenicity of IPV[a] in single or combination vaccines in developing countries or countries in transition (from developing to developed)

Reference	Country	Vaccine	Schedule	Cut-off (⩾)[b]	No. of doses	Seroconversion or seroprevalence ⩾1 month after last dose (%)		
						Type 1	Type 2	Type 3
Schatzmayr et al. (1986)	Brazil	IPV	2 m, 4 m[c]	1:5	2	99	100	100
			2 m, 4 m, 6 m	1:5	3	100	100	100
Simoes et al. (1985)	India	DTP[d]-IPV	6–7 w[e], 4 w int[f]	1:8	2	95	75	97
			6–7 w, 8 w int	1:8	2	95	83	96
			8–12 w, 4 w int	1:8	2	94	88	100
			8–12 w, 8 w int	1:8	2	100	95	100
			13–45 w, 4 w int	1:8	2	100	90	90
			13–45 w, 8 w int	1:8	2	100	100	100
Schwartz et al. (1989)	Israel	IPV	0, 6 m	1:8	2	80	98	71
Kok et al. (1992)	Kenya	DTP-IPV	2–3 m, 4–5 m	1:8	2	94	98	87
			2–3 m, 4–5 m, 6–7 m	1:8	3	100	100	98
Nirmal et al. (1998)	India	IPV intradermal	6–8 w, 8 w int	1:4	2	90	70	97
			6–8 w, 4 w int	1:4	2	90	80	98
WHO et al. (1996)	Oman[g]	DTP-IPV	6 w, 10 w	1:8	2	71	83	81
			6 w, 10 w, 14 w	1:8	3	90	96	95
	Thailand[g]	DTP-IPV	6 w, 10 w	1:8	2	40	48	79
			6 w, 10 w, 14 w	1:8	3	67	65	94
	Gambia[h]	DTP-IPV	6 w, 10 w, 14 w	1:8	3	81	82	98
Gylca et al. (2001)	Moldova	DtaP[i]-HBV[j]-IPV/sep[k] Hib[l]	6 w, 10 w, 14 w	1:8	3	99	98	99
Bordic et al. (1998)	Croatia	IPV	3 m, 4.5 m, 6 m	NA[m]	3	97	100	97
Lagos et al. (1998)	Chile	DTaP/sep IPV	2 m, 4 m, 6 m	1:5	3	100	100	100
		DTaP-IPV	2 m, 4 m, 6 m	1:5	3	100	100	100
		DTaP-IPV/sep Hib	2 m, 4 m, 6 m	1:5	3	100	100	100
		DTaP-IPV/reconstituted with Hib	2 m, 4 m, 6 m	1:5	3	100	100	100

Past Experience with ID IPV

- Nirmal *et al.* 1998 Vaccine 16, 928-931
  - 78 infants (6-8 weeks), India.
  - IPV (ImoVax) : 0.1 ml intradermal (normal dose 0.5 ml IM)
    - 2 doses at 8 week interval : **85.5**% seroconversion
    - 3 doses at 4 week interval: **89.0** % seroconversion
    - Concomitant with DTP
  - Comparison to previous study:
    - 2 doses 0.5 ml IM: **90**% seroconversion
- ID delivery of IPV may be a less expensive alternative for use in developing countries.

Seroconversion After 3 doses of IPV, Puerto Rico and Cuba

Country	6-10-14 weeks	2-4 mos	2-4-6 mos	Placebo
Puerto Rico[&]	86% P1 86% P2 97% P3		97% P1 100% P2 99% P3	
Cuba*	94% P1 83 % P2 100% P3	90% P1 89% P2 90% P3		0% P1 0% P2 0% P3

[&]Dayan GH, et al. Serologic response to IPV: A randomized clinical trial comparing 2 vaccination schedules In Puerto Rico. J infect Diseases 2007; 195:12-20

*The Cuba IPV Study Collaborative Group. Randomized, placebo-controlled trial of IPV in Cuba. N Engl J Med 2007;356:1536-44.

Studies on ID Delivery of IPV

- **Cuba**
  - In progress; randomized (but not blinded) trial; fractional dose ID IPV compared with full dose IM IPV; schedule 6, 10, 14 weeks; cord blood, and blood at 6, 10, 14, and 18 weeks (results in end-2007)
- **Oman**
  - Start (February 2007); schedule is 40 days, 3, and 5 months; followed by challenge dose of mOPV1 (results in mid-2008)

Summary/Conclusions

- An comprehensive program of work for IPV is being implemented
- The most important elements of which are:
  - 1) proof-of-principle of S-IPV;
  - 2) the Yogjakarta 5-year IPV project; and
  - 3) the evaluations of fractional IPV dose administered by needle-free devices intradermally
- WHO has published policy paper on IPV use after OPV cessation (WER -- April 2006)
- Convene Research Subcommittee – nominations are being solicited